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October 26, 2015

Ms. Leslie Kux
Associate Commissioner for Policy
U.S. Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket # FDA-2015-N-0101: Safety and Effectiveness of Health Care Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Proposed Amendment of the Tentative Final Monograph; Reopening of Administrative Record

Dear Ms. Kux:

The Association for Professionals in Infection Control and Epidemiology (APIC) appreciates the opportunity to provide comment to the Food and Drug Administration (FDA) on the *Safety and Effectiveness of Health Care Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Proposed Amendment of the Tentative Final Monograph (TFM); Reopening of Administrative Record*. We recognize that there have been significant changes since the 1994 tentative final monograph in the number and use of healthcare antiseptics. APIC applauds FDA for taking action to obtain and review new data on safety and efficacy of healthcare antiseptics in order to utilize current day evidence for industry guidance with the outcome being safety for patients and healthcare workers that use these products.

We appreciate the clarification and emphasis the FDA has provided, namely that the proposals for new safety and effectiveness data does not mean that the currently available health care antiseptic products are unsafe, or that their use should be limited or discontinued in any way. As Bessonneau and colleagues point out, the benefits of alcohol based hand rubs in healthcare settings have been established, while the potential adverse effects of passive exposure to alcohols has not been clearly defined.¹ APIC recognizes the limited data available to answer the question of what the acceptable/permissible level of alcohol exposure might be to healthcare workers. APIC applauds the rigorous assessment of the clinical evaluation studies, clinical outcome studies, in vitro studies, and the in vivo studies that were previously submitted for the currently available healthcare antiseptics in use today. We agree with the FDA that with the limitations found in those prior studies, as well as the definitive technological and scientific advances since the original studies were done, new methods of testing must be applied to measure and evaluate the safety and effectiveness of the healthcare antiseptic products currently in use.

APIC endorses the proposal to separate over-the-counter (OTC) antiseptic drug products into healthcare antiseptics and consumer antiseptics. (APIC previously provided comments on the consumer antiseptic wash proposed rule.²) We agree that consumer antiseptic products serve a distinctly different purpose than healthcare antiseptics.



While antiseptic use in a hospital setting is the main focus of this proposed rule, APIC appreciates the extension of this document to other healthcare situations outside the hospital. The evolving care continuum has resulted in the provision of high acuity healthcare services beyond the walls of the traditional hospital setting. Such circumstances include provision of high-tech infusion services in the home care setting as well as other non-traditional settings. Patients and healthcare workers in these other settings deserve the same level of safety and efficacy standards as those in the hospital setting. It will be important to better clarify and define the scope of this document in order that the proper antiseptic products are provided for patients in the spectrum of healthcare settings while also being covered by healthcare insurers. The concern is that these entities may only determine that they need to supply products intended for “consumer use”, which as indicated in this document, have different and lesser standards.

APIC appreciates the attention provided in this document related to the essential components of hospital infection control measures of which healthcare antiseptics are a core component. Providing additional clarity on the term “preoperative skin preparations” should be provided. The term as noted in the document is inclusive of skin preparation for surgical operative procedures in addition to other types of procedures such as skin preparation prior to an injection. This provides for confusion in that it could be misinterpreted that all products listed can be used for either. Generally, it would be uncommon to utilize alcohol alone as an antiseptic for skin preparation prior to a surgical procedure while it is very commonly used as a pre-injection skin prep.

While this document appears to focus on the use of antiseptics directly on the skin, it does not address the newer uses of such products (e.g. preoperative skin preparations) in healthcare since the initial 1972 tentative monograph. For example, the use of alcohol prep pads has expanded beyond the initial intended use “for preparation of the skin prior to an injection”. Delivery of medications to patients has expanded beyond skin injection whereby a considerable amount of medications are instead administered via intravascular catheters. These methods are supported by national guidelines^{3,4} and require scrubbing the end caps of intravascular tubing lines routinely and frequently with antiseptics like 70% isopropyl alcohol prep pads prior to administering medications. More recently, the application of alcohol impregnated cap covers that remain in place for extended periods of time are being used for similar purposes. Safety and efficacy considerations of these antiseptics on intravenous catheter tubing systems and understanding the level of introduction into the patient’s blood would seem prudent given this is the more common mechanism of use for such alcohol products.

The added use of chlorhexidine gluconate products for scrubbing and disinfecting IV caps prior to infusion of medications is another method currently being used in healthcare settings. We recognize chlorhexidine gluconate products are covered under New Drug Applications and are not eligible for inclusion as OTC healthcare antiseptics because they were not included in the 1994 TFM. However, we believe inclusion of safety and efficacy data including the issue of introduction of both alcohol and chlorhexidine gluconate into the blood (systemic exposure) should be addressed by human pharmacokinetic data under maximal use conditions. If such issues, either for alcohol, chlorhexidine gluconate or both, are beyond the scope of this proposed monograph, APIC recommends that this issue be investigated and addressed by FDA in order to be in line with current healthcare practices with these antiseptics.

APIC agrees with the FDA that additional data and information is needed to address the question of healthcare antiseptics and their potential role in antimicrobial resistance, and agrees with the data that



the FDA is requesting to better understand these interactions in order to develop an adequate risk assessment for healthcare antiseptic uses.

We recognize that manufacturers are aware of this proposed rule and may be working to gather the necessary testing data while the rule is in proposal, but have concerns that an effective date of one year after publication of the final rule may not allow all manufacturers to submit the necessary data. Were that to be the case, the result might be a shortage of products necessary to provide safe and effective care to individuals receiving healthcare services. Consideration should be given to a contingency plan that would address any potential shortages in healthcare antiseptics that result from manufacturers not meeting the effective date for data submission.

APIC appreciates the opportunity to review this proposed rule and provide input on behalf of our members.

Sincerely,

A handwritten signature in black ink that reads "Mary Lou Manning". The signature is written in a cursive, flowing style.

Mary Lou Manning, PhD, CRNP, CIC, FAAN, FNAP
2015 APIC President

¹ Bessonneau, V. et al., Can Intensive Use of Alcohol-Based Hand Rubs Lead to Passive Alcoholization? *International Journal of Environmental Research and Public Health*. 2010; 7;3038-3050.

² Association for Professionals in Infection Control and Epidemiology. Comment on Docket No. FDA-1975-N-0012, Safety and Effectiveness of Consumer Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Proposed Amendment of the Tentative Final Monograph; Reopening of Administrative Record March 25, 2014 Available at: http://www.apic.org/Resource/TinyMceFileManager/Advocacy-PDFs/FDA_Antimicrobial_hand_soaps_3-25-14.pdf Accessed October 8, 2015.

³ O'Grady NP, et al. Guidelines for the prevention of intravascular catheter-related infections. *AJIC* 2011;39:S1-S34.

⁴ Marschall J, et al. Strategies to prevent central line-associated bloodstream infections in acute care hospitals: 2014 Update. *ICHE* 2014;35:S89-107.